

Post Cesarean Infection: A Review

A review of post-caesarean infectious morbidity: How to prevent and treat

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Introduction

Puerperal infection is a significant cause of morbidity and mortality in postpartum women worldwide (Kassebaum et al. 2014). Puerperal infection increases length of hospital stay and healthcare costs. One of the major risk factors for postpartum infection is cesarean delivery (CD). Post cesarean infection can be separated into two sub groups: surgical site infection and endometritis. Surgical site infection (SSI) refers to infection of the skin and subcutaneous tissue at the location of the incision. Endometritis or endomyometritis refers to infection of the uterine corpus, endometrium, and myometrium. According to a large retrospective study in the United States, the cost per patient of readmission and treatment for SSI and endometritis was \$3529USD and \$3956USD respectively (Olsen et al. 2010). In addition to healthcare costs, there is the potential for impact on initiation and continuation of breastfeeding. In 2012, approximately 22.9 million CDs were performed worldwide (Molina et al. 2015); it is imperative to understand the disease process and prevention and management strategies.

Epidemiology

In developed countries, the risk of endometritis following primary CD with appropriate antibiotic prophylaxis is reported as 6% in women who have not labored and 11% in patients who have labored. Following repeat CD, the risk of endometritis is 2% (without labor) and 3% (with a trial of labor) (Hammad et al. 2014). Without antibiotic prophylaxis, risks of endometritis are estimated to be 38.5% (Gibbs et al. 1978). The risk of SSI after CD has been reported as high as 4.5% (Gibbs et al. 1978). In low resource settings, the post-cesarean wound infection rate is reported to be higher at 9.3-10.9% (Arabshahi & Koohpayezade 2006; Ezechi et al. 2009).

Risk factor identification

There are several known risk factors for postpartum wound infection including obesity, diabetes, and preexisting infection. While many risk factors have been identified for composite infectious outcomes, there have been fewer studies looking at wound infection as a specific outcome. A prospective study of a Vietnamese population identified seven risk factors for postpartum wound infection including: preoperative remote infection, chorioamnionitis, maternal preoperative condition, American Society of Anesthesiologists (ASA) score of >3 , preeclampsia, higher body mass index (BMI), nulliparity, and elevated intraoperative blood loss (Tran et al. 2000).

One of the most common identified recurrent risks of wound infection is obesity. A study by Tran et al. showed that when obesity is stratified, the odds ratio of postoperative infection increases by 2.0 per every 5-unit increment increase in BMI (Tran et al. 2000). Chauhan noted that there is greater morbidity after cesarean delivery following failed vaginal delivery in patients weighing 300 or more pounds at the time of delivery (Chauhan et al. 2001). Another study of 194 morbidly obese women (BMI of 50 or greater) found that 30% of these women had wound complications. In this same group, women who smoked, were diabetic, had subcutaneous drains, vertical incisions, or blood loss greater than 1 liter were more likely to develop postoperative wound complication (Alanis et al. 2010).

While often occurring with obesity, diabetes, specifically postoperative hyperglycemia, is an independent risk factor for postoperative wound infection in cardiac patients (Lazar et al. 2004) but has not been shown to increase rates of wound infection after cesarean delivery (Johnston et al. 2017). Johnson and colleagues evaluated 176 women with diabetes and found that although immediate postoperative hyperglycemia did not correlate with wound complication, women readmitted for wound complication did have significantly higher mean fasting blood sugar compared to women who were not (Johnston et al. 2017). In a large Danish retrospective study, Type 1 Diabetes was an independent risk

factor for post-operative wound infection after controlling for obesity and mode of CD (Leth et al. 2011). Many studies also demonstrate that obesity, commonly linked to diabetes, has a cumulative risk when paired with diabetes. One study showed that obesity in women with diabetes increased the risk of infections by more than half (OR 2.2, CI, 1.6-3.1) while combined obesity and diabetes increased the risk of infection by 9.3 (95% CI, 4.5-19.2; $P < 0.001$) (Schneid-Kofman et al. 2005).

A significant risk factor for post-cesarean wound infection is the presence of preexisting intrauterine infection or chorioamnionitis (Shree et al. 2016; Tran et al. 2000). A recent retrospective cohort study of women between 2010 and 2013 characterized 213 women with chorioamnionitis who underwent cesarean delivery. Of these women, 32 (15%) developed a wound infection. Those 32 patients were more likely to have a BMI of 40 or greater, have chronic hypertension, or use tobacco compared to the group of women who did not develop a wound infection. It appears that while chorioamnionitis is an independent risk, like obesity, it can be compounded with other risks (Dotters-Katz et al. 2016). In women undergoing cesarean delivery in the setting of chorioamnionitis, it may be reasonable to continue antibiotics beyond delivery to decrease the risk of wound infection, even if the woman is afebrile.

Prevention

As defined by the Centers for Disease Control, an infection must occur within 30 days of the operation to be classified as a SSI. In a study performed by Declercq et al., it was found that postpartum women who had undergone a planned cesarean section were 2.3 times more likely to be re-hospitalized for wound complications or infection than women who had a planned vaginal delivery (Declercq et al. 2007). In efforts to decrease the incidence of postpartum wound infection, several preventative practices have been proposed, studied, and adopted into practice.

Antibiotics

In the modern medical world, antibiotics have become an essential tool for the reduction of puerperal infections and prophylactic antibiotics are used routinely to reduce morbidity in obstetrics. A Cochrane review in 2014 explored the effect of antibiotic prophylaxis in all cesarean sections including elective and non-elective, repeat and primary, as well as preoperative and intraoperative delivery of antibiotics.

Wound infection was found to be decreased (RR 0.40; 95% CI 0.35 to 0.46) with use of antibiotics.

Subgroup analyses demonstrated that the most effective antibiotic prophylaxis agents for wound infection prevention were the extended-spectrum penicillin class (RR 0.18, 95% CI 0.09-0.39) and aminoglycoside class (RR 0.17 95% CI 0.08-0.34) (Smaill & Grivell 2014). Presently, the American College of Obstetricians and Gynecologists (ACOG) recommends administration of antimicrobial prophylaxis within 60 minutes of the start of cesarean delivery. In the case of emergent CD, antibiotics should be administered as soon as possible after the incision is made. Regimens that provide appropriate coverage are a first generation cephalosporin or a combination of aminoglycosides and clindamycin for women with a history of severe reactions to cephalosporins (ACOG 2011). A recent Cochrane review demonstrated that penicillins and cephalosporins are equivalent in prophylactic activity (Gyte et al. 2014). Choice of antibiotic therapy should be based on patient history, physician preference, local epidemiologic data regarding pathogen prevalence, and hospital data regarding antibiotic resistance.

While it is widely accepted that the use of antibiotics decreases postpartum infectious morbidity in both elective and non-elective cesarean deliveries, optimal time of antibiotic administration is unknown. In gynecologic surgeries, it is recommended that antibiotics be given an hour before the initial incision. Other considerations exist in obstetric surgeries where perinatal transfer of antibiotics to the fetus occurs. While it has been shown that intrapartum antibiotic prophylaxis changes the neonatal gut biome at one month of life (Corvaglia et al. 2016), the long term effects of neonatal exposure to antibiotics are

unknown. Maternal antibiotic administration has been shown to increase the rate of neonatal sepsis work up; however a study by Cunningham et al. did not show any increased rates of culture proven sepsis in the era prior to routine prophylactic antibiotic administration (Cunningham et al. 1983). To our knowledge, no studies exist that have evaluated the long term effects of maternal antibiotic dosing.

From the perspective of prevention of maternal infection, there is consensus on timing of maternal antibiotic administration. A Cochrane review demonstrated a significant reduction in wound infection in women who received preoperative compared to intraoperative (RR 0.59; 95% CI 0.44 to 0.81) (Mackeen et al. 2014) antibiotics. The American College of Obstetrics and Gynecology affirms this guideline and recommends antibiotics within 60 minutes of incision.

Vaginal preparation

A common etiology of post-operative wound infection, particularly endometritis, is ascending infection from the vagina. In a recent Cochrane review, vaginal preparation with povidone-iodine solution prior to cesarean delivery has been shown to decrease postpartum endometritis. This reduction in endometritis is more dramatic with women who have ruptured membranes (Haas et al. 2014). In this review, there was not a reduction in wound complications and postoperative fever. There is also theoretical risk of disrupting normal vaginal flora which may predispose the woman to bacterial vaginosis or other disturbances in vaginal pH. While not routine, vaginal preparation prior to cesarean may be considered as an adjunct to antibiotics to reduce post-operative infectious morbidity.

Skin Preparation

Skin cleansing immediately prior to skin incision is a component of standard operative protocol. Multiple agents exist; chlorhexidine and povidone-iodine are two of the most frequently used skin preparations

for abdominal surgeries. In a study by Nagi et al., the effects of these two solutions were compared. There was no difference in surgical site infection rates among chlorhexidine in alcohol, povidone-iodine in alcohol, and a mixture of the two (Nagai et al. 2015). Another study demonstrated fewer surgical site infections after using chlorhexidine-alcohol compared to iodine alcohol (RR 0.55; 95% CI 0.34-0.90). Patients with chlorhexidine skin preparation also had fewer physician office visits although rates of readmission, endometritis, and adverse skin reactions remained similar between the two groups (Methodius G Tuuli et al. 2016). These data are supported by a meta-analysis which demonstrated that chlorhexidine-alcohol skin prep had lower rates of surgical site infections than with povidone (Lee et al. 2010). Even though chlorhexidine-alcohol has a higher cost than other available agents, it is likely less expensive when taking into account the cost of prevented wound infections. It also must be allowed to dry completely if use of electrosurgical instruments is planned; this property should be especially addressed in emergent situations.

Wound Closure

Method of incision closure also influences development of postoperative wound complications. Contribution of closure of the subcutaneous layer has been investigated. In a Cochrane review published in 2004, closure of the subcutaneous layer was associated with a decrease in any type of wound complication (RR 0.68, 95%CI 0.52 to 0.88). Risk of hematoma or seroma was decreased in the closure group compared to the non-closure group (RR 0.52, 95% CI 0.33 to 0.82). There was no significant difference in the rate of wound infection compared to the rate of infection in the non-closure group. Three of the seven studies included only women with two centimeters or more of subcutaneous fat, the other four did not specify layer thickness (Anderson et al. 2004). An updated meta-analysis by Pergialiotis et al. confirmed these findings with more than double the number of patients. The likelihood

of developing a wound infection was not significantly different between the closure group and the non-closure group (OR 0.99, 95% CI 0.70 to 1.41) (Pergialiotis et al. 2017).

Type of closure material also impacts complication rate. In a meta-analysis comparing traditional metal staples to subcuticular suture, staples were associated with a significantly decreased operative time (MD -8.66 min, 95% CI -10.90 to -6.42) compared to suture. There was no difference in cosmetic outcome at 6-8 weeks. However, use of staples significantly increased incidence of wound complications compared to subcuticular suture (RR 1.88, 95% CI 1.45 to 2.45) and the suture group had improved cosmesis at 6-12 months (Wang et al. 2016). Mackeen et al. had previously demonstrated similar outcomes with a meta-analysis of 12 randomized trials. Women with incisions closed using subcuticular suture were significantly less likely to develop a wound complication (RR 0.49, 95% CI 0.28 to 0.87) and had a longer operative time (MD 7 min, 95% CI, 3.10-11.31) compared to women with incisions closed with staples (Mackeen et al. 2015). A similar result was obtained by Zaki et al. when analyzing wound complications in women with a prepregnancy BMI of 30 or greater: use of staples was associated with a higher rate of wound complications than use of subcuticular suture (adjusted RR 1.78, 95% CI 1.27 to 2.49) (Zaki et al. 2016). No significant difference in wound complications has been shown when comparing subcuticular suture to subcuticular absorbable staples (Schrufer-Poland et al. 2016), monofilament suture to braided multifilament suture (Methodius G. Tuuli et al. 2016), or subcuticular suture to skin glue (Daykan et al. 2017).

Negative Pressure Wound Therapy

Preliminary studies of single use negative pressure wound therapy devices have shown a benefit in high risk patients undergoing cesarean delivery. In a study of 110 women with at least one risk factor for postoperative complications, NPWT application resulted in a significantly lower rate of wound and infectious morbidity (21.0% vs. 6.4%, $p=0.0007$) (Swift et al. 2015). A pilot study of women with BMI of

45 or greater did not show any significant difference in wound complication after placement of traditional NPWT at the time of CD, however this study was underpowered (Mark et al. 2013). A cost-benefit analysis has shown that NPWT may be cost-beneficial in patients at high risk for wound complications (Echebiri et al. 2015).

Diagnosis of Surgical Site Infection

Because wound infections are the result of inoculation during the procedure, the pathogen(s) require time to amplify and thus the majority of wound infections are not apparent until at least postoperative day four (Faro & Faro 2008; Martens et al. 1995), with the exception of Group A Streptococcal infections, which typically occur within the first four days with most in the first one to two days (Hamilton et al. 2013). Diagnosis of surgical site infection is clinical; daily inspection and examination of the incision should be made. Vitals including temperature should also be monitored. Wound infection is characterized by spreading erythema around the incision, induration, increased warmth, and tenderness or pain at the incision site. Drainage from the wound may also be present and may be serosanguinous or purulent. Severe infections may also be evidenced by fever or other systemic signs; patients with significant wound abscesses may have cyclical spiking fevers (Owen & Andrews 1994). Wound culture is of limited usefulness in the diagnosis of post cesarean wound infection. As nearly all wounds are colonized with a polymicrobial cohort (Bowler et al. 2001), culture results will return with multiple organisms regardless of the infectious agent or severity of infection. Providers should be cognizant that the clinical picture may be confounded by the presence of endomyometritis or other infection for which the patient is already receiving antibiotics (Owen & Andrews 1994).

Treatment

Conflicting recommendations exist regarding the treatment of mild, non-purulent wound infections (cellulitis). When the area of erythema and induration extends fewer than 5 centimeters from the incision and there are no systemic signs of infection (elevated white blood cell count, fever, altered vital signs), some references suggest a course of oral antibiotics only, usually a cephalosporin (Fitzwater & Tita 2014), while others state the only course of action for any infected wound is to open the incision and debride it (Stevens et al. 2014). There is insufficient evidence to issue a final recommendation, though likely either course would be effective for mild cellulitis.

More severe infections, whether with discharge or not, should be opened completely, explored, and debrided (Cliby 2002). Sutures or staples should be removed and the entire subcutaneous space should be explored to evaluate for fluid collection (seroma or hematoma) and to ensure fascial integrity. A swab of the wound should be sent for culture and sensitivity testing to guide choice of antibiotics. The wound should be copiously irrigated and debrided with normal saline using at least 8 pounds per square inch of pressure (Stevenson et al. 1976; Tabor et al. 1998), which can be accomplished with a 35mL syringe and a 19 gauge needle (Stevenson et al. 1976). The wound should then be packed with moist gauze and dressed. Empiric antibiotic therapy should be started with a cephalosporin and metronidazole or other broad spectrum coverage suitable for genitourinary pathogens. Appropriate regimens include piperacillin-tazobactam monotherapy and ceftriaxone plus metronidazole combination therapy (Fitzwater & Tita 2014; Stevens et al. 2014). Pharmacologic therapy should be modified once the culture results are available, if necessary. Wound dressings should be changed twice daily and the incision debrided as necessary. Once the infection is cleared, the decision should be made to allow the wound to heal by secondary intent or to reclose it. Some evidence suggests that re-closure is appropriate and leads to decreased healing time with minimal risk for reoperation (Cliby 2002; Walters et al. 1990).

Preliminary evidence for the use of negative pressure wound therapy (NPWT) in the setting of infected wounds suggests a higher antibiotic concentration is achieved in wound tissue in patients receiving

NPWT compared to those receiving traditional dressings (Lo Torto et al. 2017). In another study of 20 patients with infected wounds, 19 had a favorable response to NPWT in combination with antibiotic therapy with a mean duration of antibiotic therapy of 20 days and a 29% decrease in mean wound area (95.65–68.1 cm²; $p < 0.05$) (Jones et al. 2016). Most data are obtained from patients with trauma injuries or chronic ulcers, however, a small series of 21 patients with abdominal wounds closed with mesh and with subsequent infection described the effectiveness of NPWT. Patients who received NPWT appeared to have decreased length of hospital stay, fewer procedures, and fewer readmissions compared to historical data prior to NPWT use, however this study was descriptive in nature and not designed to detect statistical differences (Baharestani & Gabriel 2011). A single patient case study of a woman who underwent a term CD and developed SSI and abscess and was treated with NPWT reports that NPWT in this setting was well tolerated and efficacious in infection resolution and wound healing (Young et al. 2016). Though there is limited data on the outcomes after NPWT use in the treatment of wound infection, preliminary reports indicate that it may be useful. NPWT should be considered when determining the treatment regimen for SSI after CD.

Patients with wound infection and sepsis need supportive therapy in addition to the therapies outlined above, which may include fluid resuscitation, blood pressure support, and multiple parenteral broad spectrum antimicrobial agents. This care may necessitate admission to an intensive care unit (ICU) and consultation with intensivists. Care should be taken to ensure appropriate dosing of antimicrobial agents if renal dysfunction is part of the clinical picture (Patel et al. 2010).

Necrotizing fasciitis is a surgical emergency. Patients found to have extensive necrosis and/or fascial dehiscence upon probing of the opened or dehiscent wound should be evaluated in the operating room to fully drain any seroma or hematoma, surgically debride the necrotic tissue, and evaluate for necrotizing processes. If necrotizing fasciitis is not evident, the decision must be made regarding fascial closure: if sufficient viable tissue is present to allow primary closure without undue tension on the

suture line, the fascia may be closed (Cliby 2002). If the fascia cannot be closed without excessive tension, a mesh bridge can be placed (Cliby 2002). Non-surgical management of fascial dehiscence is appropriate if the patient is unstable or has significant edema (Cliby 2002) but primary closure should be accomplished when possible as the occurrence of incisional hernia is nearly guaranteed if the fascia is not closed primarily (van Ramshorst et al. 2010). A small study outlines a protocol using negative pressure wound therapy to decrease the time to primary fascial closure (Suliburk et al. 2003).

Multiple wound dressing products and regimens exist, but a Cochrane review did not find any difference in healing (Vermeulen et al. 2004). The provider should choose the appropriate dressing based on wound complexity, patient ability to manage the dressing change, and availability of materials.

Uncomplicated wounds can be dressed with plain gauze and an absorbent pad, though it is important to change the dressing often enough that the packing gauze does not dry out (Svensjö et al. 2000; Ousey et al. 2016). Topical antiseptics such as Dakin's solution, iodine, and hydrogen peroxide are likely cytotoxic to healthy tissue and should be avoided (Cardile et al. 2014; Oberg 1987). Recommendations for complex wounds should be sought from a wound care team, particularly for patients with multiple medical conditions which may impair wound healing or who are taking medications such as chronic steroids which may impair wound healing.

Summary

In conclusion, post cesarean wound infection remains an important clinical problem despite advancing technologies. Diagnosis and identification of risk factors are vital in reducing maternal morbidity.

Diagnosis is largely clinical with evidence of fever, increased pain, erythema, and/or wound disruption.

Treatment usually involves antibiotics and depending on severity may require surgical exploration and more invasive therapy. Common risk factors include but are not limited to obesity, hyperglycemia, and

pre-existing skin or intrauterine infection. Prophylactic antibiotics, appropriate skin preparation, and other interventions have been proven to reduce the incidence of postoperative cesarean infectious morbidity. It is imperative to have an understanding of, prevent, and treat post-cesarean wound infection to improve the recovery and health of women and families in the postpartum period.

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